Unexpected outcome (positive or negative) including adverse drug reactions

Reactive amyloidosis complicated by end-stage renal disease
28 years after liquid silicone injection in the buttocksGeraldine d'Ythurbide,¹ Khaldoun Kerrou,² Isabelle Brocheriou,³ Alexandre Hertig^{1,4}¹Department of Urgences Néphrologiques et Transplantation Rénale, APHP, Hôpital Tenon, Paris, France²Department of Nuclear Medicine, APHP, Hôpital Tenon, Paris, France³Department of Pathology, APHP, Hôpital Tenon, Paris, France⁴Université Pierre et Marie Curie, Paris 6, France**Correspondence to** Professor Alexandre Hertig, alexandre.hertig@tnn.aphp.fr**Summary**

Silicone granulomas usually arise from the rupture of silicone implants. Until the 1980s, however, underground care providers used to inject liquid and unapproved silicone directly into human tissues, in the absence of a containing capsule. We report here the case of a man who ultimately developed end-stage renal disease (ESRD) because of a chronic glomerulosclerosis that was attributed to a glomerular AA amyloidosis diagnosed 28 years after a buttock injection of liquid silicone. To our knowledge, this is the first case of a silicone-induced AA amyloidosis irreversibly affecting the kidneys, and leading to ESRD. An interleukin 1 receptor antagonist was started to prevent the extension of amyloidosis, but to no avail as far as the kidneys are concerned. We want to draw the attention of health professionals about the risk of developing AA amyloidosis secondary to a long-lasting inflammation induced by silicone leakage, after a long latency period.

BACKGROUND

Long-term complications of silicone are now under considerable scrutiny (cf. the recent scandal of 'PIP' implants). Here, we want to draw the attention of health professionals about a new potential risk of silicone, occurring with a long latency period. Silicone fluids have been used extensively over the last 40 years, to the aim of soft tissue augmentation. It is notably offered to male-to-female trans-sexuals, to help them feminising their body. Of amazing simplicity, injection of silicone is not always medically agreed or encapsulated.

CASE PRESENTATION

A 49-year-old North African male-to-female trans-sexual patient, infected with HIV-1 under HAART therapy (913 CD4 T cells/mm³), and co-infected with hepatitis C virus (HCV), presented with general weakness. HIV and HCV viral loads were null and 9M copies/ml, respectively. His

social history was significant for oral narcotic and crack cocaine use, from which he was however deprived (and substituted by methadone since 15 years). Although serum and urinary samples taken 1 year ago showed a decreased creatinine clearance (46 ml/min) and nephrotic range proteinuria, his chronic glomerulopathy was left undiagnosed.

Physical examination was unremarkable except for the presence of peripheral oedema: the patient had neither fever nor pain, nor any symptoms suggestive of an autoinflammatory disease. Renal function was severely impaired (serum creatinine: 1173 µmol/l), with hypoalbuminaemia (8.5 g/l) and massive proteinuria (urinary protein-to-creatinine ratio: 2954 mg/mmol) without haematuria. A renal ultrasound revealed normal-sized kidneys. A Doppler ruled out a renal vein thrombosis. C reactive protein (CRP) and serum amyloid A (SAA) concentrations were mildly increased (15 and 46 mg/l, respectively). Complement C3 and C4

Figure 1 Kidney biopsy. (A) Salmon pink staining of amyloid with Congo Red (original magnification $\times 400$). Amyloid is seen in the mesangium and in the renal vasculature. (B) Immunohistochemistry for AA protein (peroxidase autoperoxidase stain for AA protein, diaminobenzidine as marker; original magnification $\times 100$). Intense staining of amyloid deposits for AA protein in the mesangium, the interstitium and vessels.

concentrations were normal, serum tested negative for anti-neutrophil cytoplasmic antibodies, antinuclear antibodies and cryoglobulin, and no monoclonal component was detected. Kidney biopsy revealed AA-amyloidosis, with complete obliteration of glomerular architecture by amyloid deposits and interstitial fibrosis (figure 1). There was no family history of familial mediterranean fever (FMF), and

no mutation was found in the FMF gene (including type 2). Therefore, we retained the diagnosis of AA amyloidosis consecutive to a chronic but clinically silent inflammation (the chronic use of methadone probably explains the absence of pain). A fluorodeoxyglucose positron emission tomography (PET)/CT revealed a hypermetabolic activity and hyperdense nodules in the gluteal area (figure 2). In

Figure 2 Fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT. 18F-FDG PET/CT images in upper plate demonstrate the increased glucose uptake (SUV maximum of 4.5) in the soft-tissues, gluteal muscles and lower back (left column: 3D Maximum Intensity Projection; upper row from left to right: transversal, sagittal and coronal PET only; bottom row: fused PET/CT). An x-ray CT transversal slice in lower plate shows multiple small and hyperdense particles made of liquid silicone.

retrospect, the patient recalled of intramuscular injections of liquid silicone for cosmetic purpose 28 years earlier (500 ml/buttock), by a qualified nurse operating in the underground milieu of Paris.

DIFFERENTIAL DIAGNOSIS

Of note, neither HIV nor HCV infection are known to induce AA amyloidosis.

TREATMENT

Excision of the exogenous material was technically impossible. Colchicine was contraindicated because of end-stage renal disease. To prevent the vascular extension of AA amyloidosis, the patient was started on sequential courses of an interleukin 1 receptor antagonist, which has shown some efficacy in FMF-related amyloidosis complicated by renal failure.¹ This drug was preferred over corticosteroids or tumour necrosis factor inhibitors for safety reasons.

OUTCOME AND FOLLOW-UP

After a follow-up of 6 months, the systemic inflammatory syndrome fully resolved (CRP was <5 mg/l and SAA was undetectable), yet haemodialysis was still required, and a PET/CT scan found a persistently high metabolism in the buttocks.

DISCUSSION

Whether the inflammation was a reaction to silicone per se, or would have occurred with any foreign material injected into the buttock—possibly as the result of recurrent trauma when sitting—is unknown. Hage *et al*² had however reported the devastating outcome of 15 male-to-female trans-sexuals injected with silicone either in the hips or in the gluteal area. After a latency period ranging from 5 months to 17 years, acute inflammation and severe fibrosis had typically developed, accompanied by changes in skin colour or texture, skin sloughs, contractures and even deformities. Systemic complications are hitherto rare, and no strong evidence has been found that silicone can cause connective tissue diseases.³ To our knowledge, only one case

of silicone-induced amyloidosis has been reported, that occurred 19 years after an augmentation mammoplasty with silicone gel-filled implants.⁴ The patient had proteinuria, but no alteration of renal function was reported, and a kidney biopsy (unshown) only mentions perivascular amyloidosis.

The worldwide use of silicone in order to increase body parts is popular since the late 1970s. Because of the surprisingly high latency period that we and others have observed, we may fear an increase in incident cases of systemic (including renal) AA amyloidosis.

Learning points

- ▶ Reactive AA amyloidosis is a potential risk of silicone injection and occurs after a long latent period.
- ▶ This risk should be known, since AA amyloidosis can be life-threatening.
- ▶ Positron emission tomography imaging is a valuable tool to identify silent inflammation in the buttock.

Competing interests None.

Patient consent Obtained.

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